41. (Amended) A D-peptide which comprises at least four amino acid residues and comprises the consensus sequence WXWL (SEQ ID NO: 23), wherein W represents D-tryptophan, L represents D-leucine and X represents any moiety.

44. (Amended) A D-peptide which comprises at least five amino acid residues, wherein the at least five amino acid residues are EWXWL (SEQ ID NO: 24), wherein E represents D-glutamic acid, W represents D-tryptophan, L represents D-leucine and X represents an amino acid residue, a modified amino acid residue or a moiety other than an amino acid residue.

Please replace the "Sequence Listing" filed on August 7, 2001(sheets 1/20 through 20/20) with the attached Substitute "Sequence Listing" (sheets 1/25 through 25/25) comprising SEQ ID NOS: 1-71.

REMARKS

This Substitute Sequence Listing and Preliminary Amendment is submitted to add listings for three sequences, SEQ ID NO: 69, SEQ ID NO: 70 and SEQ ID NO: 71. These sequences appear at page 10 of the application as filed, but were inadvertently omitted from the Sequence Listing filed on August 7, 2001. The paragraph in the specification containing these sequences has been amended to include the appropriate sequence identifiers.

In addition, certain previously listed sequences are identified in the specification as containing acetylated or amidated amino acid residues. The information regarding those acetylated or amidated amino acid residues has also been added to this Substitute Sequence Listing.

No new matter has been added as a result of these amendments. Entry is respectfully requested.

Respectfully submitted,

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MARKED UP VERSION OF AMENDMENTS

Specification Amendments Under 37 C.F.R. § 1.121(b)(1)(iii)

Replace the paragraph at page 10, lines 4 through 28, continuing to page 11, lines 1 through 8 with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

Peptides, both D-peptides and L-peptides, which fit into a deep hydrophobic pocket in the trimeric N-helix coiled-coil of HIV-1 envelope glycoprotein gp41 are also the subject of this invention. The D-peptides are the first molecules that have been shown to bind exclusively to the gp41 hydrophobic pocket. The observation that these D-peptides inhibit gp41-mediated membrane fusion processes (syncytia formation and viral infection) provides the first direct demonstration that HIV-1 infection can be inhibited by molecules that bind specifically to pocket. The validation of the gp41 hydrophobic pocket as a drug target sets the stage for the development of a new class of orally bioavailable anti-HIV drugs, that work by inhibiting viral entry into cells. Such drugs would be a useful addition to the current regimen used to treat HIV-1 infection with combination therapies. D-peptides, such as the D-peptides described herein, portions, modification and variants thereof and larger molecules (e.g., polypeptides) which comprise all or a portion of a D-peptide described herein, are useful to inhibit HIV membrane fusion and, thus, HIV entry into cells. D-peptides, corresponding to the D-amino acid version of phage sequences identified as described herein, are inhibitors of HIV-1 infection and syncytia formation. The C-terminal residues in these D-peptide inhibitors have the sequence pattern: CXXXXXEWXWLCAA-am (SEQ ID NO: 69). (In the phage-display library, the positions corresponding to the C residues were encoded as either C or S, the positions corresponding to the AA residues were encoded as such and the other 10 positions (indicated by X) were randomly encoded. The -am represents a C-terminal amide, added as part of

the peptide synthesis procedure.) The N-terminal residues in the D-peptide inhibitors are, for example, ac-GA, ac-KKGA (SEQ ID NO: 70), or ac-KKKKGA (SEQ ID NO: 71). The ac- represents an N-terminal acetyl group added as part of the peptide synthesis procedure. The C-terminal amide and the N-terminal acetyl group are optional components of D-peptides of this invention. Other N-terminal residues can be included, in place of or in addition to those in the previous sentence, as desired (e.g., to increase solubility). For example, D-peptides of the following sequences are also the subject of this invention:

ac-XXCXXXXXEWXWLCXX-am (SEQ ID NO: 28);
ac-KKXXCXXXXXEWXWLCXX-am (SEQ ID NO: 29);
ac-KKKKXXCXXXXXEWXWLCXX-am (SEQ ID NO: 30);
ac-XXCXXXXXEWXWLCXXX-am (SEQ ID NO: 31);
ac-KKXXCXXXXXEWXWLCXXX-am (SEQ ID NO: 32); and
ac-KKKKXXCXXXXXEWXWLCXXX-am (SEQ ID NO: 33).

Replace the paragraph at page 57, lines 4 through 20 with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

IQN17 and the D10 peptides were synthesized by FMOC peptide chemistry. They have an acetylated N-terminus and a C-terminal amide. IQN17 contains 29 residues derived from GCN4-pI_QI on the N-terminus and 17 residues from the C-terminus of N36 on the C-terminus. There is one residue overlap between GCN4-pI_QI and the N36 region, making the peptide 45 residues long. To improve solubility, three amino-acid substitutions were made in the GCN4-pI_QI region of IQN17, as compared to the original GCN4-pI_QI sequence (Eckert, D.M. *et al.*, *J. Mol. Biol.*,

284:859-865 1998). These substitutions are L13E, Y17K, and H18K. Thus, the sequence of IQN7 is:

ac-RMKQIEDKIEEIESKQKKIENEIARIKKLLQLTVWGIKQLQARIL-am (SEQ ID NO: 1)

(ac- represents an N-terminal acetyl group and -am represents a C-terminal amide), with the HIV portion underlined. For mirror-image phage display, IQN17 was synthesized using D-amino acids (for amino acid residues that contain a second chiral center, such as Ile and Thr, the exact mirror image of the naturally occurring amino acid residue is used to create the D-version of the target). In addition, the N-terminus of the peptide was biotinylated using NHS-LC-biotin II (Pierce, catalog #21336). Between the biotin and the IQN17 sequence was a three amino acid linker of GKG, with the lysine in the naturally-occurring L-form. This lysine was inserted as a trypsin recognition site.

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

39. (Amended) A fusion protein of Claim 38 wherein the portion of the N-peptide region of HIV gp41 comprises the following 24 amino acid residues of HIV:
SGIVQQQNNLLRAI EAQQHLLQLT (SEQ ID NO: 21).

41. (Amended) A D-peptide which comprises at least four amino acid residues and comprises the consensus sequence WXWL (SEQ ID NO: 23), wherein W represents D-tryptophan, L represents D-leucine and X represents any moiety.

44. (Amended) A D-peptide which comprises at least five amino acid residues, wherein the at least five amino acid residues are EWXWL (SEQ ID NO: 24), wherein E represents D-

glutamic acid, W represents D-tryptophan, L represents D-leucine and X represents an amino acid residue, a modified amino acid residue or a moiety other than an amino acid residue.